UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,433	08/10/2000	Mark C. Noe	PC10491A	6255

7590 02/19/2002

Paul H Ginsburg
Pfizer Inc
235 East 42nd Street 20th Floor
New York, NY 10017-5755

EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 02/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,433	NOE ET AL.	
	Examin r	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to amendments filed on 12/27/01. Applicants have amended claim 16. There are twenty-three pending claims and five under consideration. Claims 16-20 are use claims. This is the third action on the merits. All claims were previously rejected. The application concerns some inhibitors of the enzyme aggrecanase.

Response to Amendment

2. Applicants' amendment to claim 16, listing the specific diseases for which they claim treatment overcomes the indefiniteness rejection made in point #5 of the previous office action.

Election/Restrictions

3. This application contains claims 1-15 and 21-23 drawn to an invention nonelected without traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for small molecules of the formula I, does not reasonably provide enablement for all small molecules. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Applicants' claims are drawn to the use of any molecule with a specific biological property. What are the structures of these molecules and where in the specification do Applicants teach how to make this potentially limitless structural variety of such molecules?

Applicants argue that they have provided an enabling disclosure and point to the working examples in the specification. They further argue that the level of skill in organic chemistry is such that any small molecule meeting Applicants claim limitation of a molecular weight lower than 2000 can be prepared. Applicants also look to *In re Strahilevitz* 212 USPQ 561 for guidance.

Applicants' arguments are not persuasive for three reasons. Firstly, claim 16 is drawn to use of any compound, of any structure below a certain molecular weight. The claimed process does not have to be achieved by the sulfonamide compounds of Formula I. The Examiner admits that Applicants have meet their enablement and best mode requirements for the sulfonamide piperazine compounds of Formula I, page 5 of the specifications with X = nitrogen. That structural formula, however, is not a limitation to the claims presently under examination. Thus, we are uncertain of the means they claiming for their intended use. Secondly, patent law generally holds that chemical reactions are inherently

unpredictable and there is a larger burden on Applicants to provide a written description of how to obtain the compounds for which they claim use. Synthesis of the compounds is only one step required to practice claim 16. One would have to conceive of a chemical structure, devise a synthesis of it, carry out that synthesis, test the compound for its aggrecanase inhibiting prosperities, and finally ascertain if it was safe and effective for the treatment of human disease. It is the Examiner's belief that the first of those steps is the most difficult but any one of them surpasses the standard of undue experimentation.

Thirdly, *In re Strahilevitz* 212 USPQ 561 concerned use of "a hapten-removing device" to achieve a therapeutic goal. Applicants' are claiming use of compound for achieving a therapeutic goal. The issue of the structure of the device was not directly considered by the court but it did note that in finding [3] that dialysis membranes were described in the specification and the court stated the "invention resides in combining the known prior art techniques of hemodialysis or hemoperfusion ...". One can infer the court believed the "a hapten-removing device" is a machine used for hemodialysis or hemoperfusion and well known in the art. In addition the patent which arose from *In re Strahilevitz* 212 USPQ 561, Strahilevitz ('414) contains in claim 1, lines 8-18, column 13 a specific description of the device. Thus, *In re Strahilevitz* 212 USPQ 561 is not on point technically

because this was a mechanical not a chemical issue and not on point legally because the mechanical apparatus was claimed in terms more narrow than its weight and intended function, which is what Applicants are doing.

Applicants argue that *In re Fisher*, 166 USPQ 18, cited by the Examiner, was not on point to the written description rejection. They point to the open-ended nature of the Fisher claim, in contrast to their own closed limitation of molecular weight. They also argue that the level of skill in ACTH preparation is low compared to the high level of skill in treating diseases arising from articular cartilage destruction. This is not persuasive. The Applicants have considered only one of the two findings from *In re Fisher*, 166 USPQ 18 drawn to description. For completeness both holdings are quoted,

> "(e) The rejection for insufficient disclosure. The examiner did not reject the claims for insufficient disclosure. This was first applied by the board, although the board failed to denominate it a new ground of rejection under Rule 196(b). Appellant apparently did not complain of such failure, but chose to appeal here. The board stated: "[W]e consider appellant's claims to be so broad that the specification lacks sufficient supporting description to comply with the requirements of 35 U.S.C. 112 first paragraph." The board noted that the claims cover substantially all "preparations" produced synthetically or by breakdown of the 39 amino acid polypeptides in any manner to form a polypeptide product of lesser molecular weight containing any number (claim 5) or at least 24 (claim 4) of the amino acids as long as the product exhibits, without the stated side effects, activity equal to at least 1 International Unit of ACTH per milligram. We have already discussed, with respect to the parent application, the lack of teaching of how to obtain other-than-39 amino acid ACTHs. That discussion is

> fully applicable to the instant application, and we think the board was correct in finding insufficient disclosure due to this broad aspect of the claims.
>
> The second aspect of breadth mentioned by the board in the quoted portion of its opinion has not yet been discussed. This is the problem arising from the potency recitation "at least 1 International Unit of ACTH per milligram." This is a so-called "open-ended" recitation. It has a lower limit but no upper limit. As previously mentioned, the specification discloses products having potencies from 111% to 230% of standard, which we understand to mean from 1.11 to 2.30 International Units of ACTH activity per milligram. The issue thus presented is whether an inventor who is the first to achieve a potency of greater than 1.0 for certain types of compositions, which potency was long desired because of its beneficial effect on humans, should be allowed to dominate all such compositions having potencies greater than 1.0, including future compositions having potencies far in excess of those obtainable from his teachings plus ordinary skill."

It is the breadth and open-ended nature of Applicants' compound structural limitation to which the Examiner objects.

To quote from the MPEP §2164.03 " In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work." Thus, it is not correct for Applicants to

assert that articular cartilage destruction therapy or aggrecanase enzymology are predictable arts.

Applicants made no traversal of the Examiners application of *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016, *Oka,* 849 F.2d at 583, 7 USPQ2d at 1171, *Genentech Inc v. The Wellcome Foundation Ltd.*, 31 USPQ2d 1161, *Fiers v. Sugano*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), or *Burroughs Wellcome Co. v. Barr Laboratories Inc.,* 32 USPQ2d 1915 to the present enablement issue.

5. Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What are the chemical formulas of the molecules whose use Applicants claim? The number of "small molecules" having a molecular weight of less than 2000 grams/mole is infinite.

The Applicants argue their two limitations characterizing the "small molecule" i.e. size and biologically function are sufficient to define what they claim and that names and/or chemical formulas are not required. This is not persuasive. It is an important principle of chemical patent law that a compound be described sufficiently so that a potential infringer will be able to determine the metes and bounds of the claims. A chemical whose structure is not determinable

with present technology may be patented if sufficient number of its properties have been recited to insure unique characterization of the compound. So may a compound be claimed by the process used if it is made clear what is the structure. Neither of those two exceptions applies to the present application. Surely, Applicants do not maintain that the technology exists to examine a chemical structure drawn on a piece of paper and determine its ability to inhibit the enzyme aggrecanase without making and testing the compound? Nor can Applicants claim that the technology exists to take the structure of an enzyme and determine *a priori* the structure of every possible inhibitor of that enzyme. Thus, a potential infringer would not understand what chemical structures are covered by Applicants claim limitations. The Board of Patent Appeals and Interference held in *Ex parte PULVARI* 157 USPQ 169 "a material defined, as here, solely in terms of what it can do, of a property thereof or of the scientific principle that underlies that property, ... [does not] particularly point out, as required by 35 U.S.C. 112, appellant's disclosed invention, which in the instant case would be that mixtures of certain materials have a desirable property."

Claim Rejections - 35 USC § 102

6. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson ('361). The passage spanning line 66, column 1 to line 6 column 2 of this reference teaches aggrecanase inhibitory activity. Claim 15 of the reference

lists treatment of specific diseases, which include Applicants' limitation "destruction of articular cartilage".

7. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Reiter ('392). Lines 1-8, column 1 of this reference teaches aggrecanase inhibitory activity. Claim 7 of the reference lists treatment of specific diseases, which include Applicants' limitation "destruction of articular cartilage".

8. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Duan ('336). Lines 43-46, column 238 of this reference teaches aggrecanase inhibitory activity. Claims 9-12 of the reference lists treatment of general diseases, which include Applicants' limitation "destruction of articular cartilage".

Applicants argue that the three references do not disclose the binding affinities required by Applicants claim limitation "IC_{50} of less than about 20 nM". Therefore, Applicants argue that all of Applicants claim limitations are not met by the disclosure of the references. This is not persuasive. The three references cited by the Examiner are silent as to the potencies of the disclosed compounds. The testing methods are taught by the references but no results. For all the Examiner knows, the compounds taught in Robinson ('361), Reiter ('392), and Duan ('336) do have the required potency.